

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁵ : B01D 71/02	A1	(11) International Publication Number: WO 93/23154 (43) International Publication Date: 25 November 1993 (25.11.93)
<p>(21) International Application Number: PCT/EP93/01280</p> <p>(22) International Filing Date: 19 May 1993 (19.05.93)</p> <p>(30) Priority data: 9200902 21 May 1992 (21.05.92) NL</p> <p>(71)(72) Applicant and Inventor: VAN RIJN, Cornelis, Johannes, Maria [NL/NL]; Gerard Doustraat 10, NL-1072 VP Amsterdam (NL).</p> <p>(74) Agents: HOOIVELD, Arjen, Jan, Winfried et al.; Trenité Van Doorne, P.O. Box 75265, NL-1070 AG Amsterdam (NL).</p>		<p>(81) Designated States: JP, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p>Published <i>With international search report.</i></p>
<p>(54) Title: INORGANIC MEMBRANE FOR MICROFILTRATION, AND A PROCESS FOR PRODUCTION OF SUCH AN INORGANIC MEMBRANE</p> <div data-bbox="560 1302 1047 1543" data-label="Image"> </div> <p>(57) Abstract</p> <p>The inorganic membrane consists of a macroporous inorganic support and an inorganic membrane layer. The membrane layer is formed through depositing an inorganic layer by "Chemical Vapour Deposition" or "sputtering" on the macroporous support, onto this inorganic layer a photo-lacquer layer is formed, this photo-lacquer layer being exposed to a regular mask pattern with the use of a suitable source, this lacquer layer being developed, and in the inorganic layer the mask pattern is etched by a suitable etchant, thus forming the membrane layer. The pattern of the membrane layer may be given any particularly design, practically with a repetition rate in the range 0.1-10 μm. It is thus conceivable to separate not only particles according to their size, but also to their shape. The membrane layer can be deposited very thinly in comparison to the dimension of the pore size, enabling a large flux, a reduced clogging and a minimal damage to particles or cells.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	FR	France	MR	Mauritania
AU	Australia	GA	Gabon	MW	Malawi
BB	Barbados	GB	United Kingdom	NL	Netherlands
BE	Belgium	GN	Guinea	NO	Norway
BF	Burkina Faso	GR	Greece	NZ	New Zealand
BG	Bulgaria	HU	Hungary	PL	Poland
BJ	Benin	IE	Ireland	PT	Portugal
BR	Brazil	IT	Italy	RO	Romania
CA	Canada	JP	Japan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SK	Slovak Republic
CI	Côte d'Ivoire	LI	Liechtenstein	SN	Senegal
CM	Cameroon	LK	Sri Lanka	SU	Soviet Union
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	MC	Monaco	TG	Togo
DE	Germany	MG	Madagascar	UA	Ukraine
DK	Denmark	ML	Mali	US	United States of America
ES	Spain	MN	Mongolia	VN	Viet Nam
FI	Finland				

Inorganic membrane for microfiltration, and a process for production of such an inorganic membrane.

5 The present invention relates to an inorganic membrane for microfiltration, that consists of a macroporous inorganic support and an inorganic membrane layer with pores having a pore size typically between 0.01 μm and 10 μm , which membrane layer is connected rigidly to the inorganic support. The invention relates also to a process for production of such an inorganic membrane.

10 A membrane consisting of a macroporous support and a membrane layer is a composite membrane. The macroporous support contributes here to the mechanical strength of the total membrane. Whenever the membrane layer with a high pore density is deposited relatively thinly in comparison to the mean pore size on a relatively thick support a membrane with a high flux is obtained. In case the inorganic membrane layer as well as the
15 inorganic support is made of suitable ceramic materials then the membrane will be chemically highly inert and will operate well at elevated temperatures.

From EP-A-0 144 097 a composite ceramic membrane is known having above mentioned characteristics. Said ceramic membrane has a membrane layer that is formed by coating a
20 porous support with a film by immersion in a stable sol of colloidal metal oxide ($\gamma\text{-ALOOH}$) particles and then drying and heating the support, thus forming a microporous membrane layer of metal oxide particles.

Such known inorganic membranes may display mechanical faults, like little fractures and 'pinholes' with typical size 10 μm to 100 μm , which are relatively large in comparison to the
25 mean pore size, typically 5 nm - 5 μm , thus reducing the separating characteristics.

Another intrinsic disadvantage of these membranes is the relatively large thickness of the membrane layer in comparison to the mean pore size, resulting in reduced flux characteristics of the membrane. In said patent application the thickness of the membrane layer ranges from 50 to 1000 times the mean pore size of the membrane layer.

The present invention has as an object to provide an inorganic membrane with improved separating and flux characteristics. An other object is to provide an inorganic membrane particularly useful for biomedical microfiltration, in particular solutions with vulnerable cells. Said object is attained with an inorganic membrane, characterized in that the pores of
5 the membrane layer are perforations shaped as shallow channels, square to the membrane layer, in which the channels have a length and a diameter, such that the length is at least smaller than ten times the diameter of these channels.

The length of the channels then compares to the thickness of the membrane layer. The membrane layer is according to the invention thinner than ten times the diameter of the
10 channels. Because of the low length/diameter ratio of the channels an inorganic membrane with a high flux is obtained. In addition through this measure vulnerable cells have a minimum chance in being damaged during passing these channels.

The inorganic membrane may easily be produced by firstly depositing a suitable inorganic layer by evaporation or Chemical Vapour Deposition on the inorganic support, and
15 secondly making perforations in this inorganic layer by means of a suitable etching process. According to the invention an inorganic membrane is manufactured, in which the perforations in the membrane layer are made by means of a lithographic etching process, in particular UV lithography in combination with chemical etching. On the inorganic layer a photo-lacquer layer is formed, this photo-lacquer layer being exposed to a regular mask
20 pattern with the use of a suitable source, this lacquer layer being developed, then in the inorganic layer the mask pattern is etched by a suitable wet or dry etchant, thus forming the membrane layer. The use of a lithographic etching process offers the advantage that the shape of the cross-section of the channels may be designed according to demand. Long shaped rectangular cross-section will lead to high flux.

25 The pattern of the membrane layer may be given any particular design, practically with a repetition rate in the range 0.1-10 μm . It is thus conceivable to separate not only particles according to their size, but also to their shape. This may be particularly useful for the separation of biological cells, e.g. yeast or blood cells.

Appropriate materials for the membrane layer of the inorganic membrane are according to the invention composed of ceramic constituents like silicondioxide, siliconnitride, siliconcarbide, alumina, zirconiumoxide, titaniumoxide and titaniumnitride or other metal-oxides, nitrides or silicides. Other materials like carbon, silicon, or metals like gold, silver, chromium, cobalt, nickel, aluminium, titanium etc. are also appropriate. For biomedical microfiltration, e.g. separation of bloodcomponents, biocompatibel or bloodcompatibel materials may be used like titanium, titaniumnitride, chromium alloys, carbon, siliconcarbide, silicon, siliconnitride or other appropriate semiconducting materials and noble metals.

Good filtration results are obtained according to the invention with an inorganic membrane consisting of a porous support of alumina with mean pore size in the range 0.25-25 μm and an inorganic membrane layer of silicondioxide with channels of 0.05-5 μm . In preference the support and the membrane layer are constituted from equivalent materials with the same inorganic components. An inorganic membrane is thus obtained applicable in a broad temperature range with a good cohesion between the support and the membrane layer.

In preference a process for production of an inorganic membrane according to the invention is characterized in that, before the inorganic layer is deposited on the support, primarily a suitable flattening material is deposited on a surface of the support, filling all pores lying at the surface of the support. By depositing the flattening material on the porous support a reasonable uniform flat and dense surface is obtained. Useful deposition methods are vapour deposition, chemical vapour deposition, sputtering, sol/gel coating for small pores and spray coating, sol/gel coating, use of rubbing compounds, etc. for large pores. The inorganic layer deposited on a flat and dense surface will exhibit an almost featureless surface morphology, whilst the microstructure of an inorganic layer deposited directly, e.g. by means of chemical vapour deposition, on the porous support may consist of clusters of grains tightly packed together. A flat surface morphology of the inorganic layer is important in relation to the precision in which the channels may be formed by the subsequent

lithographic etching. Materials like silicon and aluminium are suitable as a flattening material, especially polysilicon is well capable in filling pores. The flattening material should in a later stage of the process be removed from the pores in the support in order to obtain a permeable membrane. In preference the flattening material is removed by means of a material selective etchant that is brought into contact with the flattening material through the yet formed membrane layer. The selective etchant should mainly attack the flattening material and hardly the support material or the inorganic membrane layer.

Another preferential process in producing the membrane according to the invention is characterized in that subsequent to the deposit of the flattening material on the support a supplementing flattening process is being performed. The flattening process may be a mechanic polishing method for a relatively rough surface. For a relatively smooth surface, the flattening process may also according to the invention be characterized in that on a surface of the flattening material firstly a thin lacquer layer is deposited, which lacquer layer will be hardened such that a very smooth surface is obtained. Secondly the hardened lacquer layer with a smooth surface is etched, such that all lacquer layer will be removed, including part of the flattening material and the support, thus obtaining a very smooth and dense support surface with filled pores. The etching of the lacquer layer may be achieved by reactive ion (plasma) etching.

The invention will now be explained by means of the accompanying drawing in which:

Figure 1 shows in cross-section a part of the inorganic membrane according to the invention.

Figures 2 and 3 show in cross-section part of the inorganic membrane according to some preferential examples according to the invention.

Figures 4 to 9 show in cross-section subsequent stages of a process for production of the inorganic membrane according to the invention.

Figures 10 to 16 show in cross-section subsequent stages of a preferential process for production of the inorganic membrane according to the invention.

The figures are schematized and are not drawn on scale. Similar parts may have the same reference-mark.

Figure 1 shows schematic in cross-section a part of the inorganic membrane according to the invention. The inorganic membrane consists of a macro-porous inorganic support 1, in this example a wafer of α -alumina with thickness 2.5 mm and mean pore size 5 μm and an inorganic membrane layer 2 of silicondioxide with thickness 2 μm . The perforations in the membrane layer 2 are shaped as shallow channels 3, square to the membrane layer 2, in which the channels 3 have a length at least smaller than ten times the diameter of the channels 3. The channels 3 are formed here with a diameter of 1 μm in the membrane layer 2. The length of the channels 3 is here two times the diameter of the channels 3. The shape of the cross-section of the channels 3 is here circular.

Depending on the application other shapes for the cross-section of the channels 3 may be chosen. For example rectangular shape, figure 2 or with line pattern shape, figure 3. Rectangular shape has the advantage that particles have difficulty in closing the channels totally. Line pattern shape of the membrane layer has the potential of a high flux. Circular or round shape of the cross-section has an advantage in separating media with vulnerable particles, in particular shallow channels with a rounded and smooth morphology are appropriate for separating biological cells.

20

Figures 4 to 9 show in cross-section subsequent stages of a process for production of the inorganic membrane consisting of a macroporous inorganic support and an inorganic membrane layer according to the invention. Prior to the deposition of the inorganic layer 4 the pores lying at the surface of the inorganic support have been flattened and filled by rubbing for example a fine siliconpowder 7 on the surface, and if necessary followed by a light polishing method, figure 4. On the flattened surface of the inorganic support 1, figure 4, in this example a wafer of siliconcarbide with thickness 2.5 mm and mean pore size 15 μm , an inorganic layer 4 of siliconnitride with thickness 3 μm is deposited by means of a suitable deposition method, here by means of 'Chemical Vapour Deposition', figure 5. The

inorganic layer 4 is formed by chemical deposition of dichlorosilane and ammonia at low pressure (LPCVD). In the inorganic layer 4 then perforations are formed through the use of a lithographic determined etching process. On the inorganic layer 4 a photo-lacquer layer 5 is formed, figure 6, in this example Eastman Kodak Resist KPR-820. The photo-lacquer layer 5 is then being exposed to a regular pattern, figure 7, with the use of a suitable UV source, here with a Nikon NSR-1010i3 projection system and with the use of a mask 6 that is projected five times reduced. The pattern of the mask is made here of round fields with a diameter of 15 μm . Subsequent the lacquer layer 5 is developed and etched leaving a reduced(5x) mask pattern of photo-lacquer 5 on the inorganic layer 4, figure 8, according to standard lithographic methods. In the inorganic layer 4 then the reduced mask pattern is etched by a suitable etchant, forming perforations with a diameter of 3 μm , herewith forming the inorganic membrane layer 4, figure 8, 9. In this example the inorganic layer 4 of siliconnitride is etched by means of a stabilized fluoro-hydrogen (HF) solution. Perforations, shaped as shallow channels 3 with square cross-section are thus formed in the inorganic layer 4. Through these yet formed channels 3 the silicon powder 7 is selectively etched with tetramethylammoniumhydride. Finally all lacquer residus are removed and a clean inorganic membrane layer 4, figure 9, is obtained.

Figures 10 to 16 show in cross-section subsequent stages of a preferential process for production of the inorganic membrane according to the invention. Before the inorganic layer 4 is deposited on a surface of the support 1 primarily a suitable flattening material 7 is deposited on the surface of the support 1 filling all pores lying at the surface of the support, 1, figure 10. The thickness of the flattening material 7 is related to the mean pore size of the porous support 1, in order to fill all pores lying at the surface of the support 1. In this example a porous support 1 of alumina with mean pore size 2 μm has as flattening material 7 a polysilicon layer with a thickness of about 5 μm . The polysilicon layer 7 is deposited on the support by disintegration of silane (SiH_4) at low pressure (LPCVD). Other materials like alumina with a well porefilling capability may also be used. After the polysilicon deposition in preference a supplementing flattening process is performed. A mechanical polish with diamond powder will do very well.

In preference according to the invention subsequent to the deposition of the flattening material 7 on the support 1 the flattening process is firstly performed by depositing on a surface of the flattening material 7 a thin lacquer layer 8, figure 11. For a thin, uniform and smooth lacquer surface 9 the method of 'spin-coating' may be employed. Next the lacquer layer 8 is hardened
5 yielding a very smooth surface 9. Then the hardened lacquer layer 8 is etched, such that all lacquer layer 8 will be removed, including part of the flattening material 7 and the support 1, herewith obtaining a very smooth and dense support-surface 10 with filled pores, figure 12. The lacquer layer 8, the flattening material 7 and a part of the support 1 is well etched with a plasma containing tetrafluoromethane(CF₄) and oxygen, resulting in a very smooth surface 10
10 with an overall surface roughness less than 0.1 μm .

Next an inorganic layer 4 of silicondioxide with thickness 1 μm is deposited by means of a suitable deposition method, here by disintegration of tetraethoxysilane, (C₂H₅O)₄Si, at low pressure (LPCVD). figure 13, on the smooth surface 10, resulting in an overall surface roughness less than 0.15 μm . On the inorganic layer 4 a photo-lacquer layer 5 is formed
15 with a thickness of about 1 μm , figure 14, by means of 'spin-coating'. The photo-lacquer layer 5 is then exposed to a regular pattern with the use of a mask 6. The pattern of the mask is made here of square fields with a size of 1 to 1 μm . The focusing depth of the projection system used is here at least 1 μm , it should be larger than the sum of the thickness of the photo-lacquer layer and the surface roughness of the inorganic layer 4.
20 Subsequently the lacquer layer 5 is developed and etched leaving a reduced(5x) mask pattern of photo-lacquer 5 on the inorganic layer 4, according to standard lithographic methods. In the inorganic layer 4 then the reduced mask pattern is etched by a suitable etchant, forming perforations with a square cross-section of 0.2 by 0.2 μm , herewith forming the inorganic membrane layer 4, figure 15. In this example the inorganic layer 4 of
25 silicondioxide is etched by means of a stabilized fluoro-hydrogen (HF) solution. The etching stops as soon as the surface 10 of the support has been reached. Excellent cylindrical perforations may also be etched by means of anisotropic reactive ion etching. Next the flattening material 7 is removed from the pores in the support 1 by means of a material selective etchant that is brought into contact with the flattening material 7 through

the perforations of the yet formed inorganic membrane layer 4, figure 15, 16. As a selective etchant, capable of etching very well polysilicon and hardly silicondioxide or alumina a plasma may be used containing at least oxygen in an amount of 1-10 % per mol and chlorine (Cl) in an amount of 25-30 % per mol.

5

From the above it may be clear that the present invention is not limited to the mentioned examples, but that for the skilled specialist many variations of the invention will be possible. For instance, for the material of the inorganic membrane layer 4 other inorganic components like sodiumoxyde, potassiumoxyde, calciumoxyde, magnesiumoxyde or silicon, gallium, arsenic, or other semiconductors and metals may be applied. The inorganic layer 4 or the support 1 may also be constituted from or coated with a biocompatible material. Other materials than polysilicon and aluminium are also possible for the use of a good flattening material 7, for example an at low temperature liquifying glasslayer. The use of the flattening material 7 for obtaining a flat and smooth surface may also be circumvented, for example through a partial liquification of the inorganic layer 4. Components may also be applied in enhancing the joining strength and temperature durability between the support 1 and the inorganic membrane layer 4, for example borax and diphosphoruspentoxyde. The formed pattern in the lacquer layer 5 and subsequently in the membrane layer 4 is not limited to the use of an external mask, but may also be shaped by means of an interference pattern or with the use of a modulated laser beam. The invention is also not restricted to the use of optical lithography, other techniques with higher resolution (submicron), like Electron Beam and X-Ray Lithography are likewise appropriate.

25

CLAIMS

1. Inorganic membrane for microfiltration, wherein the membrane consists of a macroporous inorganic support and an inorganic membrane layer with pores having a pore size, typically between $0.01\mu\text{m}$ and $10\mu\text{m}$, which membrane layer is connected rigidly to the inorganic support, characterized in that the pores of the membrane layer are perforations shaped as shallow channels, square to the membrane layer, in which the channels have a length and a diameter, such that the length is at least smaller than ten times the diameter of the channels.
2. Inorganic membrane according to claim 1. characterized in that in the membrane layer channels are formed with a diameter in the range $0.05\text{--}5\mu\text{m}$ and that the inorganic macroporous support has mean pore size in the range $0.25\text{--}25\mu\text{m}$.
3. Inorganic membrane according to claim 1 or 2. characterized in that the inorganic membrane layer is composed of ceramic constituents like silicodioxide, siliconnitride, siliconcarbide, alumina, zirconiumoxide, titaniumoxide and titaniumnitride.
4. Inorganic membrane according to claim 1 or 2. characterized in that the inorganic membrane layer is composed of metals like gold, silver, chromium, cobalt, nickel, aluminium and titanium.
5. Inorganic membrane according to claim 1 or 2. characterized in that the support and the membrane layer are constituted from biocompatibel materials like titanium, titaniumnitride, chromium alloys, carbon, siliconcarbide, silicon, siliconnitride.
6. Inorganic membrane according to claim 1 or 2. characterized in that the support and the membrane layer are constituted from equivalent materials with the same inorganic components, favorably alumina, silicodioxide or siliconcarbide.

7. Process for production of an inorganic membrane for microfiltration, wherein the membrane consists of a macroporous inorganic support and an inorganic membrane layer characterized in that an inorganic layer is deposited on a flattened surface of the support by means of a suitable deposition method and that the inorganic membrane layer is
5 formed by etching perforations in the inorganic layer.

8. Process for production of an inorganic membrane according to claim 7., characterized in that on the inorganic layer a photo-lacquer layer is formed, this photo-lacquer layer being exposed to a regular pattern with the use of a suitable source, this
10 lacquer layer being developed, that in the inorganic layer the mask pattern is etched by a suitable etchant, forming perforations shaped as channels, square to the inorganic layer, thus forming the inorganic membrane layer.

9. Process for production of an inorganic membrane according to claim 7 or 8.,
15 characterized in that the inorganic layer is deposited on the support by means of 'Chemical Vapour Deposition' or 'sputtering'.

10. Process for production of an inorganic membrane according to claim 7, 8 or 9., characterized in that before the inorganic layer is deposited on the flattened surface of
20 the support, primarily a suitable flattening material is deposited on a surface of the support, filling all pores lying at the surface of the support, which flattening material will at least be partially removed after the forming of the inorganic membrane layer.

11. Process for production of an inorganic membrane according to claim 10.,
25 characterized in that the flattening material is polysilicon, silicon or aluminium.

12. Process for production of an inorganic membrane according to claim 10 or 11.,
characterized in that the flattening material is removed after the forming of the inorganic
membrane layer by means of a material selective etchant that is brought into contact with the
5 flattening material through the perforations of the formed inorganic membrane layer.

13. Process for production of an inorganic membrane according to claim 10, 11 or 12.,
characterized in that after the deposition of the flattening material on the support a
supplementing flattening process is performed.

10

14. Process for production of an inorganic membrane according to claim 13.,
characterized in that the flattening process is performed by depositing on a surface of the
flattening material firstly a thin lacquer layer, which lacquer layer will be hardened such that a
very smooth surface is obtained., that the hardened lacquer layer with a smooth surface is being
15 etched, such that all lacquer layer will be removed, including part of the flattening material and
the support, herewith obtaining a very smooth and dense support surface with filled pores.

15. Process for production of an inorganic membrane according to claim 7 to 14.,
characterized in that the inorganic membrane layer is coated with a biocompatibel material
20 by means of a vapour deposition method.

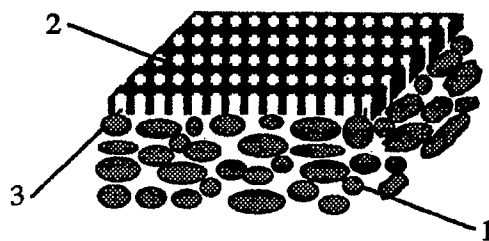


Figure 1

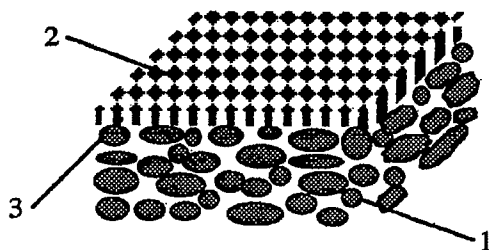


Figure 2

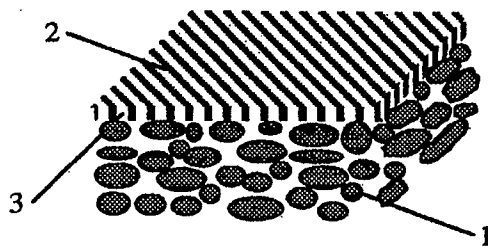


Figure 3

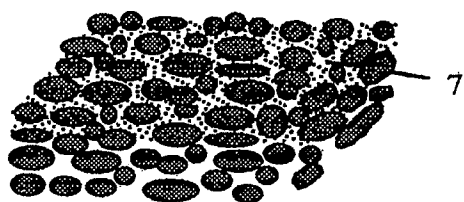


Figure 4

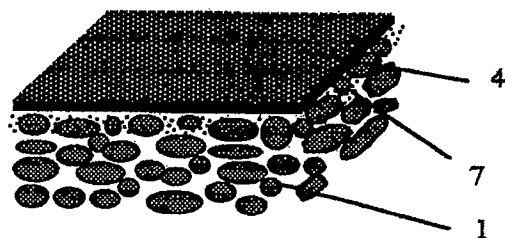


Figure 5

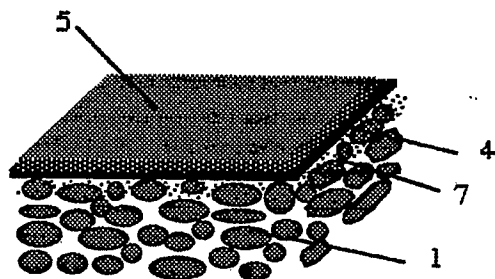


Figure 6

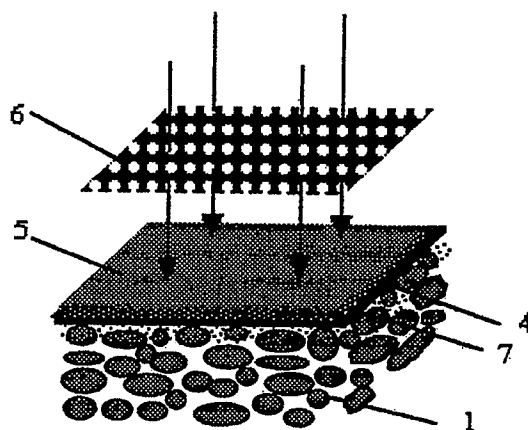


Figure 7

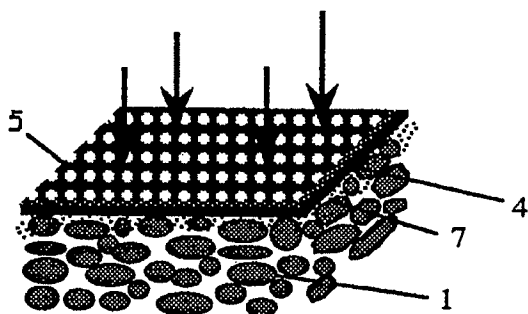


Figure 8

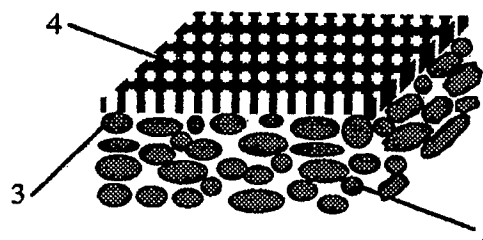


Figure 9

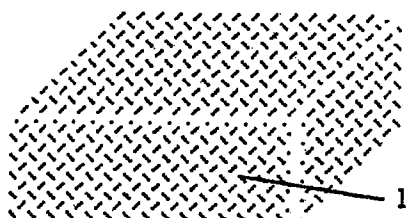


Figure 4

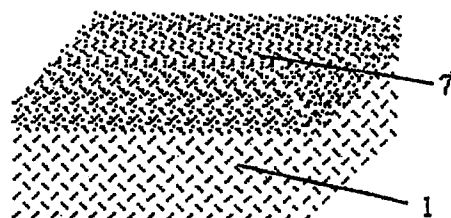


Figure 10

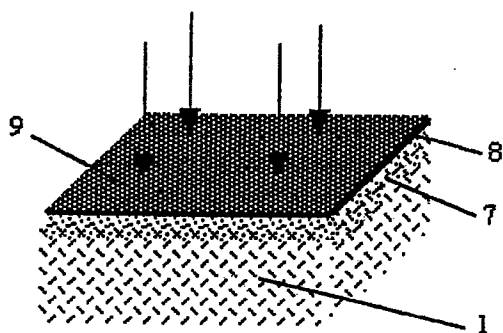


Figure 11

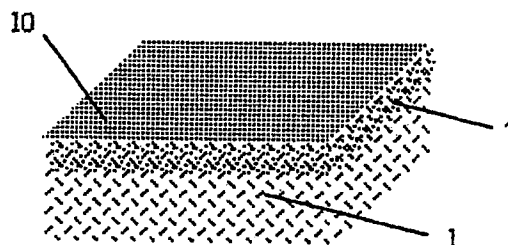


Figure 12

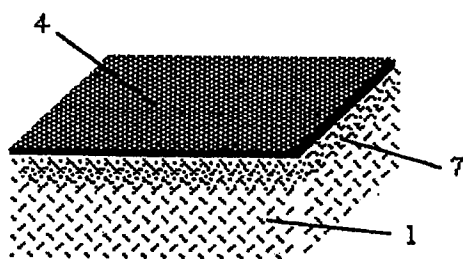


Figure 13

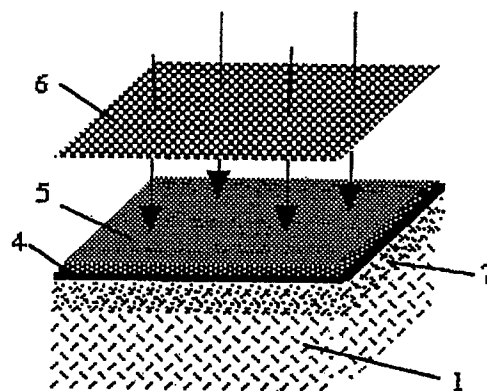


Figure 14

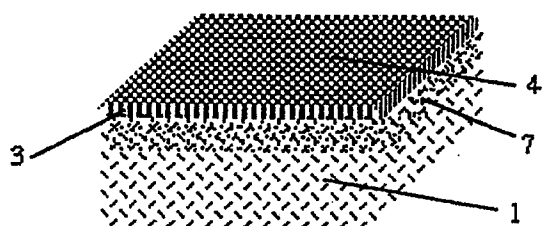


Figure 15

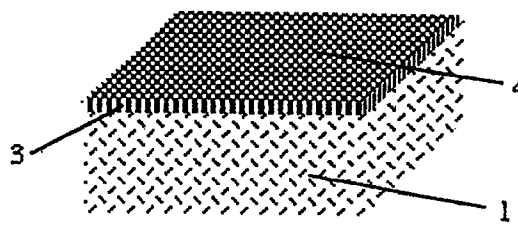


Figure 16

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 93/01280

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶		
According to International Patent Classification (IPC) or to both National Classification and IPC Int.Cl. 5 B01D71/02		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
Int.Cl. 5	B01D	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹		
Category ¹⁰	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
A	FR,A,2 336 963 (B. SCHILLING) 29 July 1977 see the whole document ---	1
A	US,A,3 794 174 (G. L. BOOMAN ET AL.) 26 February 1974 see the whole document ---	1
A	DE,A,3 524 799 (E. KRIMMEL ET AL.) 22 January 1987 see the whole document ---	1
A	EP,A,0 325 752 (AKZO N.V.) 2 August 1989 see the whole document ---	1
-/--		
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> ¹⁰ Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed </div> <div style="width: 45%;"> "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family </div> </div>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search		Date of Mailing of this International Search Report
09 JULY 1993		29. 07. 93
International Searching Authority		Signature of Authorized Officer
EUROPEAN PATENT OFFICE		DEVISME F.R.

Form PCT/ISA/210 (second sheet) (January 1985)

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
A	NUCLEAR INSTRUMENTS & METHODS IN PHYSICS RESEARCH vol. B19/, no. III?, February 1987, pages 204 - 208 P. SIOSHANSI 'MEDICAL APPLICATIONS OF ION BEAM PROCESSES' see page 3, left column, line 5-7; figure 3	1
A	FR,A,2 596 289 (BRONZAVIA-AIR EQUIPEMENT ET AL.) 2 October 1987 see the whole document	10

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.**

EP 9301280
SA 74543

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information. 09/07/93

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
FR-A-2336963	29-07-77	DE-A- 2559332	07-07-77
		DE-A- 2658405	06-07-78
		CH-A- 618612	15-08-80
		JP-A- 52097291	15-08-77
		NL-A- 7614603	04-07-77
		US-A- 4141838	27-02-79

US-A-3794174	26-02-74	None	

DE-A-3524799	22-01-87	None	

EP-A-0325752	02-08-89	DE-A- 3742770	29-06-89
		JP-A- 2043927	14-02-90
		US-A- 4923608	08-05-90

FR-A-2596289	02-10-87	GB-A, B 2190102	11-11-87
		JP-A- 63023713	01-02-88
		SE-B- 465859	11-11-91
		SE-A- 8701264	29-09-87

EPO FORM P003

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82